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TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371			U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 10/070435
INTERNATIONAL APPLICATION NO. PCT/JP00/06399	INTERNATIONAL FILING DATE 20 September 2000	PRIORITY DATE CLAIMED 20 September 1999	
TITLE OF INVENTION METHOD FOR PRODUCING CYCLIC LACTIC ACID OLIGOMER			
APPLICANT(S) FOR DO/EO/US Mikio WATANABE, Jiro TAKANO, Yoshimi ISHIHARA and Masahiro MURAKAMI			
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information.			
<p>1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)).</p> <p>4. <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).</p> <p>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)).</p> <p>a. <input checked="" type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</p> <p>b. <input checked="" type="checkbox"/> has been communicated by the International Bureau.</p> <p>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</p> <p>6. <input checked="" type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2)).</p> <p>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</p> <p>b. <input type="checkbox"/> have been communicated by the International Bureau.</p> <p>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</p> <p>d. <input checked="" type="checkbox"/> have not been made and will not be made.</p> <p>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>"UNEXECUTED"</p> <p>10. <input checked="" type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (U.S.C. 371(c)(5)).</p>			
Items 11 to 16 below concern other document(s) or information included:			
11. Assignee: <u>AMATO PHARMACEUTICAL PRODUCTS, LTD., of Kyoto, JAPAN</u>			
12. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.			
13. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.			
14. <input checked="" type="checkbox"/> A FIRST preliminary amendment.			
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17. <input checked="" type="checkbox"/> Figure of Drawing to be published <u>1</u>			
18. <input checked="" type="checkbox"/> Other items or information:			
<p>International Application as published in Japanese</p> <p>Cover Letter under 35 U.S.C. 371 AND 37 C.F.R. 1.495</p> <p>PCT/IPEA/409 International Preliminary Examination Report.</p> <p>PCT/ISA/210 (in English & Japanese).</p> <p>PCT/IB/301.</p> <p>PCT/IB/304</p> <p>PCT/IB/308.</p> <p>PCT/IB/332</p> <p>PCT/IB/338</p> <p>PCT/IPEA/408 Written Opinion</p> <p>PCT/IB/306.</p> <p>PCT/RO/101 PCT REQUEST (with International Application as filed in Japanese).</p> <p>Claim of Priority</p>			

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : M. WATANABE et al.

Appl. No :Not Yet Assigned
(U.S. National Phase of PCT/JP00/06399)

I.A. Filed: 20 September 2000

For : METHOD FOR PRODUCING CYCLIC LACTIC ACID OLIGOMER

**COVER LETTER ACCOMPANYING U.S. NATIONAL STAGE PATENT
APPLICATION FILED UNDER 35 U.S.C. 371
AND 37 C.F.R. 1.495**

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

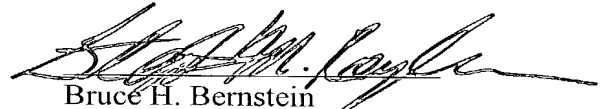
Enclosed is a new National Stage patent application for filing in the U.S. Patent and Trademark Office under 35 U.S.C. 371 and 37 C.F.R. 1.495. The Declaration and Power of Attorney attached thereto are in unexecuted form. A properly executed Declaration and Power of Attorney will be filed within the period of time set in a Notification to be mailed by the United States Patent and Trademark Office.

Related to this, a correspondence address is provided in
the unexecuted Declaration and Power of Attorney, and is as follows:

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If there any questions pertaining to this National Stage Application, please contact the undersigned.

Respectfully submitted,
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Mikio WATANABE et al.

Serial No : Not Yet Assigned (National Stage of PCT/JP00/006399)

Filed : Concurrently Herewith (International Filing Date 20 September 2000)

For : METHOD FOR PRODUCING CYCLIC LACTIC ACID OLIGOMER

PRELIMINARY AMENDMENT

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to calculation of the filing fees and the examination of the above-identified patent application on the merits, the Examiner is respectfully requested to amend the claims as follows:

IN THE CLAIMS

Please amend claims 3-6 and 9-11, as follows (a marked-up copy of the amendment is provided in the attached Appendix):

3. (Amended) The method for producing a cyclic lactic acid oligomer according to claim 1, wherein in the first heating process (i), lactic acids are subjected to dehydration condensation reaction by heating to a temperature ranging from 120°C to 140°C under a pressure of 350 to 400mmHg.

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4. (Amended), The method for producing a cyclic lactic acid oligomer according to claim 1, wherein in the second heating process (ii), the reaction product from the first heating process is heated to 145°C or higher, the reaction pressure is reduced to 100mmHg or lower at a depressurization rate of 0.5 to 1 mmHg/min, and the reaction is further continued under the reduced pressure and at a temperature of 145°C or higher so as to generate a dehydrated condensate of lactic acid.

5. (Amended) The method for producing a cyclic lactic acid oligomer according to claim 1, wherein in the second heating process (ii), the reaction product from the first heating process is heated to 150°C to 160°C, and while the reaction pressure is reduced to 15 to 20mmHg at a depressurization rate of 0.5 to 1mmHg/min, by-product water is removed by distillation while avoiding distillation of lactides, and after the reaction pressure is reduced to 15 to 20mmHg, the reaction is further continued under the same pressure and at a reaction temperature of 150°C to 160°C so as to generate a dehydrated condensate of lactic acid.

6. (Amended) The method for producing a cyclic lactic acid oligomer according to claim 1, which further comprises:
(iii) a third heating process for generating a cyclic lactic acid oligomer, which comprises a cyclization of a chain lactic acid oligomer in the reaction product from said second heating process by heating under a pressure lower than that of said second heating process.

9. (Amended) The method for producing a cyclic lactic acid oligomer according to claim 1, wherein cyclic lactic acid oligomers are selectively produced while substantially no chain lactic acid oligomers are produced.

**APPENDIX
MARKED-UP COPY OF CLAIM AMENDMENTS**

3. (Amended) The method for producing a cyclic lactic acid oligomer according to [claim 1 or 2] claim 1, wherein in the first heating process (i), lactic acids are subjected to dehydration condensation reaction by heating to a temperature ranging from 120°C to 140°C under a pressure of 350 to 400mmHg.

4. (Amended) The method for producing a cyclic lactic acid oligomer according to [any one of claims 1 to 3] claim 1, wherein in the second heating process (ii), the reaction product from the first heating process is heated to 145°C or higher, the reaction pressure is reduced to 100mmHg or lower at a depressurization rate of 0.5 to 1 mmHg/min, and the reaction is further continued under the reduced pressure and at a temperature of 145°C or higher so as to generate a dehydrated condensate of lactic acid.

5. (Amended) The method for producing a cyclic lactic acid oligomer according to [any one of claims 1 to 4] claim 1, wherein in the second heating process (ii), the reaction product from the first heating process is heated to 150°C to 160°C, and while the reaction pressure is reduced to 15 to 20mmHg at a depressurization rate of 0.5 to 1 mmHg/min, by-product water is removed by distillation while avoiding distillation of lactides, and after the reaction pressure is reduced to 15 to 20mmHg, the reaction is further continued under the same pressure and at a reaction temperature of 150°C to 160°C so as to generate a dehydrated condensate of lactic acid.

6. (Amended) The method for producing a cyclic lactic acid oligomer according to [any one of claims 1 to 5] claim 1, which further comprises:
(iii) a third heating process for generating a cyclic lactic acid oligomer, which comprises a cyclization of a chain lactic acid oligomer in the reaction product from said second heating process by heating under a pressure lower than that of said second heating process.

9. (Amended) The method for producing a cyclic lactic acid oligomer according to [any one of claims 1 to 8] claim 1, wherein cyclic lactic acid oligomers are selectively produced while substantially no chain lactic acid oligomers are produced.

10. (Amended) The method for producing a cyclic lactic acid oligomer according to [any one of claims 1 to 9] claim 1, wherein the ratio of cyclic lactic acid oligomers to total lactic acid oligomers in the reaction product is 80% by weight or more.

[illegible]

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11. (Amended) A cyclic lactic acid oligomer produced by the method for producing a cyclic lactic acid oligomer according to [any one of claims 1 to 10] claim 1.

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DESCRIPTION

METHOD FOR PRODUCING CYCLIC LACTIC ACID OLIGOMER

TECHNICAL FIELD

The present invention relates to a method for producing a cyclic lactic acid oligomer, and a cyclic lactic acid oligomer produced by the production method.

BACKGROUND ART

There is known a method for producing a lactic acid oligomer by dehydration condensation reaction of lactic acids under reduced pressure. Lactic acid oligomers obtained by this method comprise both chain oligomers and cyclic oligomers.

As a method for obtaining cyclic oligomers, there is known a method which comprises, during dehydration condensation reaction of lactic acids, heating at 145°C for 3 hours under normal pressure, reducing pressure to 150mmHg, heating for 3 hours under the reduced pressure, and then heating at 185°C for 1.5 hours under a pressure of 3mmHg (Japanese Patent Application Laying-Open (kokai) No. 9-227383).

In this method, however, the generation yield of cyclic oligomers is low, and there still remains some room for improvement of the yield.

DISCLOSURE OF THE INVENTION

The object of the present invention is to provide a novel method for producing cyclic lactic acid oligomers at a high yield, and to provide a cyclic lactic acid oligomer produced by said method.

As a result of focused research to achieve the aforementioned object, the present inventors have found that a cyclic lactic acid oligomer can be produced at a high yield by dehydration condensation reaction of lactic acids under conditions of a certain pressure and a certain temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides, thereby providing the present invention.

Thus, according to the present invention, there is provided a method for producing a cyclic lactic acid oligomer, which comprises:

- (i) a first heating process for dehydration condensation of lactic acids by heating, which comprises dehydration condensation of lactic acids under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides; and
- (ii) a second heating process for generating a dehydrated condensate of lactic acid, which comprises heating the reaction product from said first heating process to a temperature higher than that of the first heating process, reducing the pressure to 100mmHg or lower under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides, and further continuing the reaction by heating under the reduced pressure.

Preferably, in the first heating process (i), lactic acids are subjected to dehydration condensation reaction by heating to a temperature of 150°C or lower under a pressure of 10 to 760mmHg. More preferably, in the first heating process (i), lactic acids are subjected to dehydration condensation reaction by heating to a temperature ranging from 120°C to 140°C under a pressure of 350 to 400mmHg.

Preferably, in the second heating process (ii), the reaction product from the first heating process is heated to 145°C or higher, the reaction pressure is reduced to 100mmHg or lower at a depressurization rate of 0.5 to 1mmHg/min, and the reaction is further continued under the reduced pressure and at a temperature of 145°C or higher so as to generate a dehydrated condensate of lactic acid. More preferably, in the second heating process (ii), the reaction product from the first heating process is heated to 150°C to 160°C, and while the reaction pressure is reduced to 15 to 20mmHg at a depressurization rate of 0.5 to 1mmHg/min, by-product water is removed by distillation while avoiding distillation of lactides, and after the reaction pressure is reduced to 15 to 20mmHg, the reaction is further continued under the same pressure and at a reaction temperature of 150°C to 160°C so as to generate a dehydrated condensate of lactic acid

Preferably, the method for producing a cyclic lactic acid oligomer according

to the present invention further comprises:

(iii) a third heating process for generating a cyclic lactic acid oligomer, which comprises cyclization of a chain lactic acid oligomer in the reaction product from said second heating process by heating under a pressure lower than that of said second heating process.

Preferably, in the third heating process (iii), the reaction product from the second heating process is heated at 150°C to 160°C under a pressure of 0.1 to 5mmHg.

According to the particularly preferred embodiment of the present invention, there is provided a method for producing a cyclic lactic acid oligomer, which comprises:

(i) a first heating process, which comprises heating lactic acids to a temperature ranging from 120°C to 140°C under a pressure of 350 to 400mmHg for dehydration condensation reaction, while removing by-product water by distillation, and avoiding distillation of lactides;

(ii) a second heating process, which comprises heating the reaction product from said first heating process to a temperature of 150°C to 160°C, reducing the reaction pressure to 15 to 20mmHg at a depressurization rate of 0.5 to 1mmHg/min, removing by-product water by distillation while avoiding distillation of lactides, and after the reaction pressure is reduced to 15 to 20mmHg, further continuing the reaction under the same pressure and at a reaction temperature of 150°C to 160°C so as to generate a dehydrated condensate of lactic acid; and

(iii) a third heating process, which comprises cyclizing a chain lactic acid oligomer in the reaction product from said second heating process by heating at 150°C to 160°C under a pressure of 0.1 to 5mmHg so as to generate a cyclic oligomer.

In a preferred embodiment of the present invention, cyclic lactic acid oligomers are selectively produced while substantially no chain lactic acid oligomers are produced. Preferably in this case, the ratio of cyclic lactic acid oligomers to total lactic acid oligomers in the reaction product is 80% by weight or more.

According to another aspect of the present invention, there is provided a cyclic lactic acid oligomer produced by the method for producing a cyclic lactic acid

oligomer of the present invention. Preferably there is provided a cyclic lactic acid oligomer which is substantially free of chain lactic acid oligomers.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows an MS spectrum of the reaction product obtained by Example 1.

Figure 2 shows a general view of NMR of the reaction product obtained by Example 1.

Figure 3 shows a partial scale view of Figure 2.

Figure 4 shows a partial scale view of Figure 2.

THE BEST MODE FOR CARRYING OUT THE INVENTION

Embodiments and methods for carrying out the present invention are described in detail below.

The method for producing a cyclic lactic acid oligomer of the present invention comprises:

- (i) a first heating process for dehydration condensation of lactic acids by heating, which comprises dehydration condensation of lactic acids under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides; and
- (ii) a second heating process for generating a dehydrated condensate of lactic acid, which comprises heating the reaction product from said first heating process to a temperature higher than that of the first heating process, reducing the pressure to 100mmHg or lower under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides, and further continuing the reaction by heating under the reduced pressure.

The lactic acid used as a raw material in the present invention may be any one of D-lactic acid, L-lactic acid and DL-lactic acid, and these lactic acids may also be used alone or in combination of two or more.

[illegible]

After the reaction pressure is reduced to 100mmHg or lower, the reaction is further continued at this reaction pressure. The reaction period of this case is 3 to 12 hours, preferably 5 to 6 hours.

In a preferred embodiment of the present invention, a third heating process is carried out after completion of the aforementioned second heating process. The third heating process is a process where a chain lactic acid oligomer in the reaction product from the second heating process is cyclized by heating at a pressure still lower than that of the second heating process so as to generate a cyclic lactic acid oligomer.

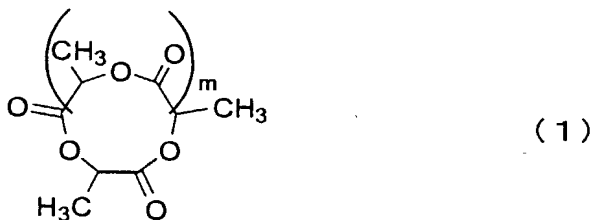
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[illegible]

The reaction is continuously performed under such pressure and temperature conditions. The reaction period is 3 to 12 hours, preferably 5 to 6 hours. By-product water generated in this case is also removed by distillation. In this case, it is preferable to avoid distillation of lactides, but it is not necessary to set the depressurization rate especially low since almost no lactides are contained in the reaction product.

The reaction of the third heating process generates a cyclic lactic acid oligomer having an average polymerization degree of 3 to 30, preferably 3 to 23. The ratio of cyclic lactic acid oligomers to total lactic acid oligomers in the reaction product from the third heating process is generally 90% by weight or more, and preferably 99% by weight or more.

The cyclic lactic acid oligomer produced by the method of the present invention is assumed to have the following chemical structure:



wherein m is an integer of 1 to 28, and preferably m is an integer of 1 to 19.

In a preferred embodiment of the method for producing a cyclic lactic acid oligomer of the present invention, cyclic lactic acid oligomers can selectively be produced while substantially no chain lactic acid oligomers are produced. The term "substantially no chain lactic acid oligomers are produced" is used herein to mean that the ratio of cyclic lactic acid oligomers to total lactic acid oligomers in a reaction product is 80% by weight or more, preferably 90% by weight or more, more preferably 95% by weight or more, and particularly preferably 99% by weight or more.

The present invention also relates to a cyclic lactic acid oligomer produced by the aforementioned method for producing a cyclic lactic acid of the present invention.

EXAMPLES

Example 1.

10.0g of (s)-(+)-lactic acid was placed in a 100ml (internal volume) eggplant-shaped flask, which was then set on a rotary evaporator. The pressure in the flask was controlled to be 350 to 400mmHg, and the flask was heated to 140°C, followed by reaction at the same pressure and the same temperature for 6 hours (the first heating process). By-product water generated from this reaction was removed by distillation. Almost no lactides were removed by distillation outside the system under the above reaction conditions.

Then, the reaction temperature was raised to 150 to 160°C, and the reaction pressure was gradually reduced from 400mmHg to 15 to 20mmHg over about 6 hours (depressurization rate: 1mmHg/min). At this depressurization rate, by-product water was removed by distillation, but almost no lactides were removed by distillation. After that, the pressure was maintained at 15 to 20mmHg and the reaction was continuously performed for 6 hours (the second heating process).

Subsequently, the pressure was reduced to 1 to 3mmHg over 30 minutes, and then the reaction was continuously performed at a reaction temperature of 160°C for 5 hours (the third heating process).

After completion of the reaction, the reaction product was analyzed and as a result, there was obtained 6.80g (yield 85%) of cyclic oligomer having an average polymerization degree of 3 to 21.

An MS spectrum of the reaction product obtained in Example 1 is shown in Figure 1. A general view of NMR of the reaction product obtained in Example 1 is shown in Figure 2, and partial scale views of Figure 2 are shown in Figures 3 and 4.

Example 2.

10.0g of (s)-(+)-lactic acid was placed in a 100ml (internal volume) eggplant-shaped flask, which was then set on a rotary evaporator. The pressure in the

flask was controlled to be 760mmHg, and the flask was heated to 140°C, followed by reaction at the same pressure and the same temperature for 10 hours (the first heating process). By-product water generated from this reaction was removed by distillation. Almost no lactides were removed by distillation outside the system under the above reaction conditions.

Then, the reaction temperature was raised to 150 to 160°C, and the reaction pressure was gradually reduced from 760mmHg to 15 to 20mmHg over about 12 hours (depressurization rate: 1mmHg/min). At this depressurization rate, by-product water was removed by distillation, but almost no lactides were removed by distillation. After that, the pressure was maintained at 15 to 20mmHg and the reaction was continuously performed for 6 hours (the second heating process).

After completion of the reaction, the reaction product was analyzed and as a result, there was obtained 6.80g (yield 85%) of cyclic oligomer having an average polymerization degree of 3 to 21.

Example 3.

Then, the reaction temperature was raised to 150 to 160°C, and the reaction

pressure was gradually reduced from 400mmHg to 70mmHg over about 5.5 hours (depressurization rate: 1mmHg/min). At this depressurization rate, by-product water was removed by distillation, but almost no lactides were removed by distillation. After that, the pressure was maintained at 70mmHg and the reaction was continuously performed for 10 hours (the second heating process).

Subsequently, the pressure was reduced to 1 to 3mmHg over 70 minutes, and then the reaction was continuously performed at a reaction temperature of 160°C for 5 hours (the third heating process).

After completion of the reaction, the reaction product was analyzed and as a result, there was obtained 6.80g (yield 85%) of cyclic oligomer having an average polymerization degree of 3 to 21.

An MS spectrum and NMR of the reaction product obtained in Example 3 were the same as those of the reaction product obtained in Example 1.

Comparison Example 1.

Comparison Example 1 was carried out in the same manner as in Example 1 with the exception that depressurization rate in the second heating process was set to be 5mmHg/min. In the depressurization operation, lactides were removed by distillation with by-product water, and as a result, the yield of cyclic oligomer was decreased to 60%.

INDUSTRIAL APPLICABILITY

According to the present invention, a cyclic lactic acid oligomer having an average polymerization degree of 3 to 30, preferably 3 to 21, can be produced at a high yield from lactic acids without using a catalyst. Moreover, a cyclic lactic acid oligomer produced by the production method of the present invention is useful as a tumor cell growth inhibiting agent, antineoplastic agent, preventive agent against cancer metastasis, QOL improving agent for cancer patients, immune activating agent, therapeutic agent for diabetes, antiobestic agent, a agent for promoting glycogen

accumulation or an agent for enhancing physical fitness. Furthermore, the cyclic lactic acid oligomer is useful not only as a medicament, but also as various types of health foods and diet supplements including soft drinks, drinkable preparations, health foods, specific hygienic foods, functional foods, function activating foods, nutritional supplementary foods, supplements, feed, feed additives, and the like.

CLAIMS

1. A method for producing a cyclic lactic acid oligomer, which comprises:
(i) a first heating process for dehydration condensation of lactic acids by heating, which comprises dehydration condensation of lactic acids under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides; and
(ii) a second heating process for generating a dehydrated condensate of lactic acid, which comprises heating the reaction product from said first heating process to a temperature higher than that of the first heating process, reducing the pressure to 100mmHg or lower under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides, and further continuing the reaction by heating under the reduced pressure.
2. The method for producing a cyclic lactic acid oligomer according to claim 1, wherein in the first heating process (i), lactic acids are subjected to dehydration condensation reaction by heating to a temperature of 150°C or lower under a pressure of 10 to 760mmHg.
3. The method for producing a cyclic lactic acid oligomer according to claim 1 or 2, wherein in the first heating process (i), lactic acids are subjected to dehydration condensation reaction by heating to a temperature ranging from 120°C to 140°C under a pressure of 350 to 400mmHg.
4. The method for producing a cyclic lactic acid oligomer according to any one of claims 1 to 3, wherein in the second heating process (ii), the reaction product from the first heating process is heated to 145°C or higher, the reaction pressure is reduced to 100mmHg or lower at a depressurization rate of 0.5 to 1mmHg/min, and the reaction is further continued under the reduced pressure and at a temperature of 145°C or higher so as to generate a dehydrated condensate of lactic acid.

to 15 to 20mmHg at a depressurization rate of 0.5 to 1mmHg/min, removing by-product water by distillation while avoiding distillation of lactides, and after the reaction pressure is reduced to 15 to 20mmHg, further continuing the reaction under the same pressure and at a reaction temperature of 150°C to 160°C so as to generate a dehydrated condensate of lactic acid; and

9. The method for producing a cyclic lactic acid oligomer according to any one of claims 1 to 8, wherein cyclic lactic acid oligomers are selectively produced while substantially no chain lactic acid oligomers are produced.

11. A cyclic lactic acid oligomer produced by the method for producing a cyclic lactic acid oligomer according to any one of claims 1 to 10.

ABSTRACT

The object of the present invention is to provide a novel method for producing cyclic lactic acid oligomers at a high yield, and to provide a cyclic lactic acid oligomer produced by said method. According to the present invention, there is provided a method for producing a cyclic lactic acid oligomer, which comprises:

- (i) a first heating process for dehydration condensation of lactic acids by heating, which comprises dehydration condensation of lactic acids under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides; and
- (ii) a second heating process for generating a dehydrated condensate of lactic acid, which comprises heating the reaction product from said first heating process to a temperature higher than that of the first heating process, reducing the pressure to 100mmHg or lower under conditions of a pressure and a temperature which allow by-product water to be removed by distillation while avoiding distillation of lactides, and further continuing the reaction by heating under the reduced pressure; as well as a cyclic lactic acid oligomer produced by said production method.

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[続葉有]

(54) Title: PROCESS FOR THE PREPARATION OF CYCLIC LACTIC ACID OLIGOMERS

(54) 発明の名称: 環状乳酸オリゴマーの製造方法

(57) Abstract: A process for the preparation of cyclic lactic acid oligomers, which comprises (i) the first heating step of condensing lactic acid through dehydration by heating under such conditions of pressure and temperature that by-product water can be distilled away while avoiding the distillation-off of lactide, and (ii) the second heating step of lowering the pressure of the resulting reaction system to 100mmHg or below at a temperature higher than that of the first step under such conditions of pressure and temperature that by-product water can be distilled away while avoiding the distillation-off of lactide, and further continuing the reaction under the resulting lowered pressure by heating to form a condensate of lactic acid; and cyclic lactic acid oligomers prepared by the process.

(57) 要約:

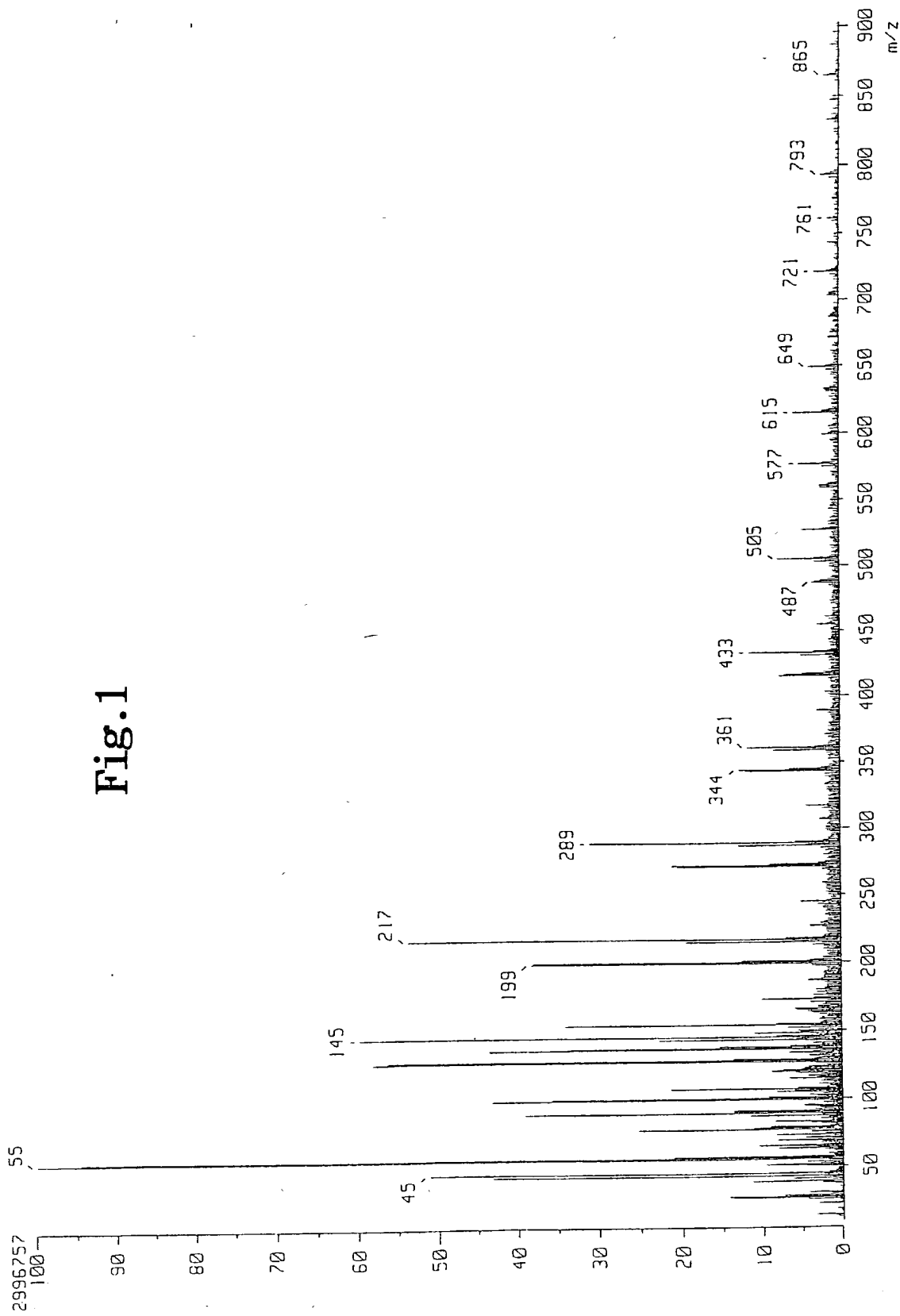
本発明によれば、(i)乳酸を加熱により脱水縮合する工程であって、ラクチドの留出を回避しつつ副生水を留出除去するような圧力及び温度条件下で脱水縮合する第1加熱工程;及び

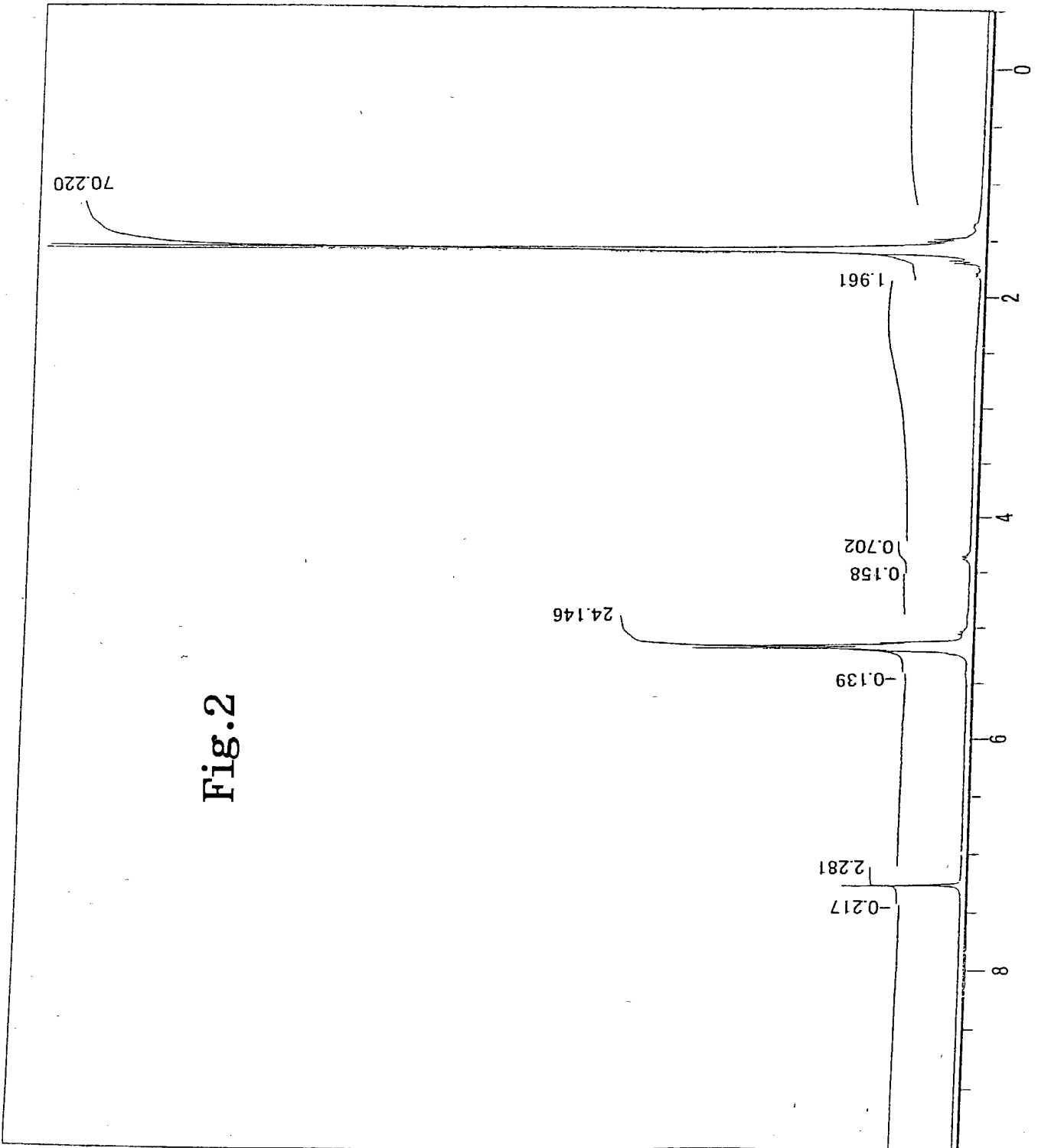
(ii)該第1加熱工程の反応生成物を、第1加熱工程より高い温度において、ラクチドの留出を回避しつつ副生水を留出除去するような圧力及び温度条件下で圧力を100mmHg以下まで降下させ、該降下した圧力において加熱下においてさらに反応を継続して乳酸の脱水縮合物を生成させる第2加熱工程、

を含む環状乳酸オリゴマーの製造方法、並びに該製造方法により製造される環状乳酸オリゴマーが提供される。

WO 01/21613 A1

Fig. 1





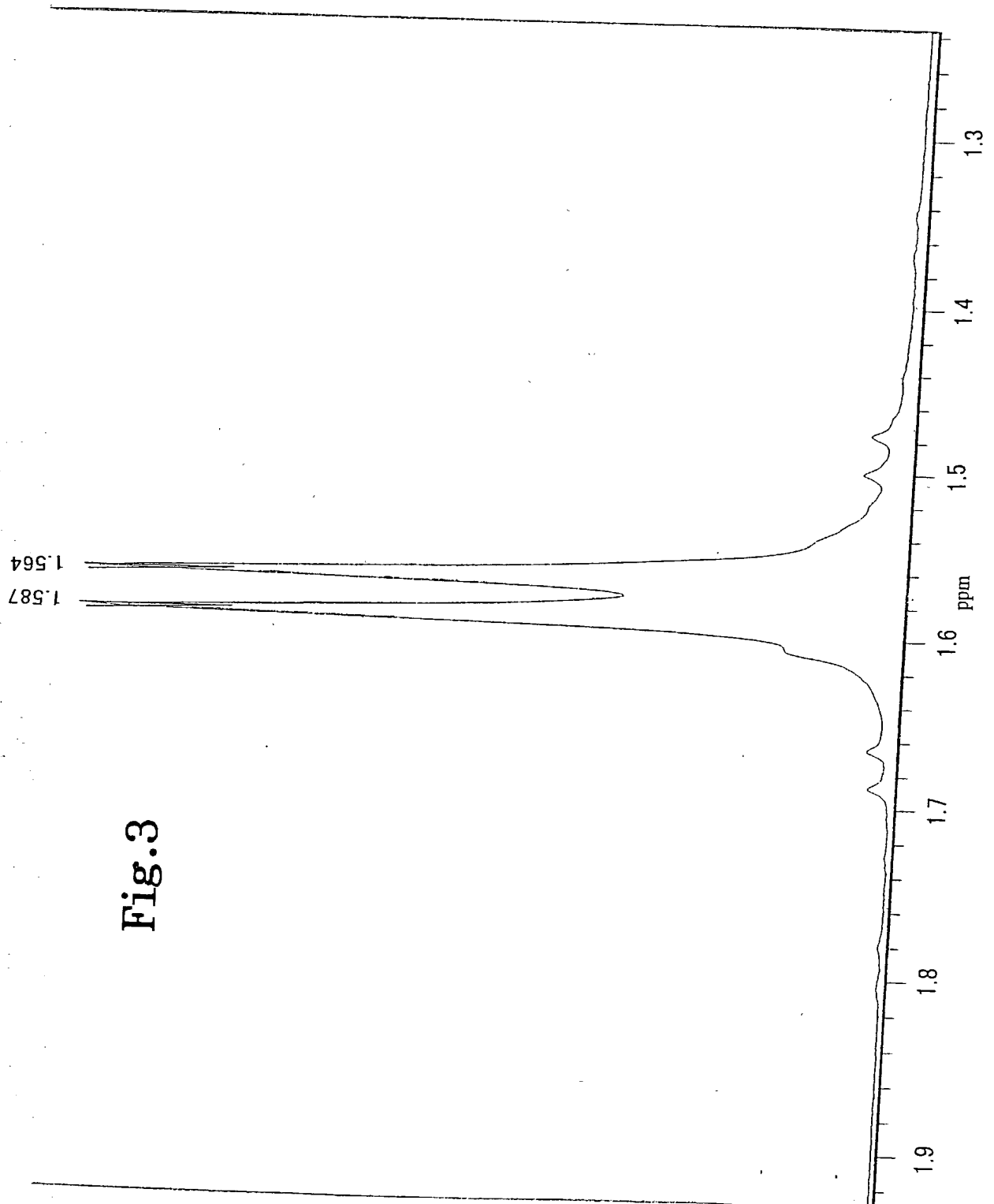


Fig.3

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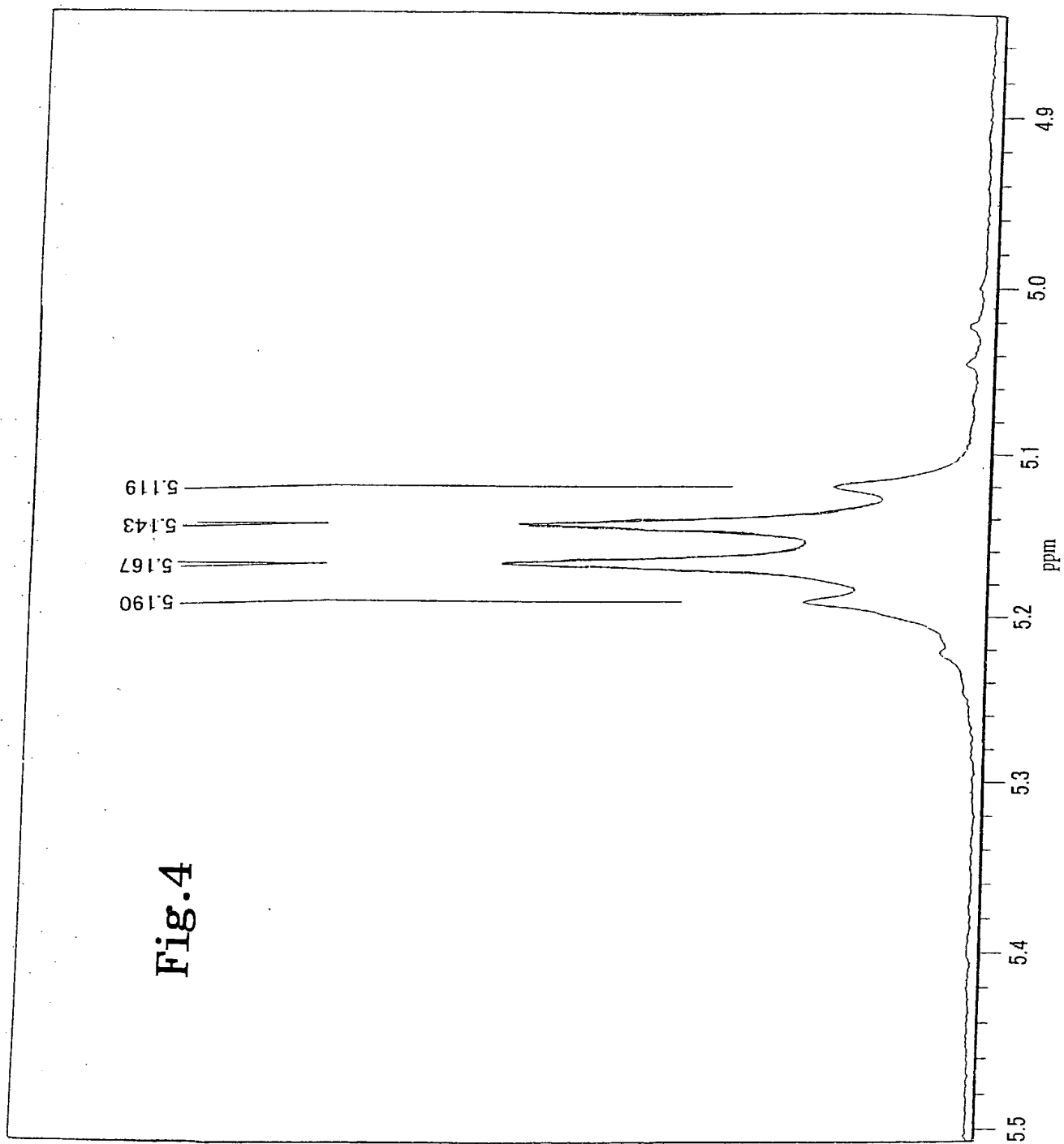


Fig.4

25 JUN 2002

10/010435

Declaration and Power of Attorney for Utility or Design Patent Application

特許出願宣言書

Japanese Language Declaration

私は、下欄に氏名を記載した発明者として、以下のとおり宣言する：

私の住所、郵便の宛先および国籍は、下欄に氏名に続いて記載したとおりであり、

名称の発明に関し、請求の範囲に記載した特許を求める主題の本来の、最初にして唯一の発明者である（一人の氏名のみが下欄に記載されている場合）か、もしくは本来の、最初にして共同の発明者である（複数の氏名が下欄に記載されている場合）と信じ、

上記発明の明細書（下記の欄で x 印がついていない場合は、本書に添付）は、

☐ 年 月 日に提出され、米国出願番号
とし、（該当する場合）
年 月 日に訂正されました。又は、

特許協定条約国際出願番号 とし、
（該当する場合） 年 月 日に訂正されました。

私は、前記のとおり補正した請求の範囲を含む前記明細書の内容を検討し、理解したことを陳述する。

私は、連邦規則法典第 37 編第 1 条 56 項に定義されているとおり、特許資格の有無について重要な情報を開示すべき義務があることを認めます。

私は、合衆国法典第 35 部第 119 条 (a-d) 項又は第 365 条 (b) 項に基づく、下記の外国特許出願又は発明者証出願、或いは第 365 条 (a) 項に基づく、少なくとも米国以外の 1 カ国を指名した PCT 国際出願の外国優先権を主張し、更に優先権の主張に係わる基礎出願の出願日前の出願日を有する外国特許出願、又は発明者証出願或るいは PCT 国際出願を以下に“なし”の箱に印をつけることにより明記する。

Prior foreign applications
先の外国出願

11-265732 (Number) (番号)	Japan (Country) (国名)	20/Sep/99 (Day/Month/Year Filed) (出願の年月日)
(Number) (番号)	(Country) (国名)	(Day/Month/Year Filed) (出願の年月日)

☐ その他の外国特許出願番号は別紙の追補優先権欄にて記載する。

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name:

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

Method for Producing Cyclic Lactic Acid Oligomer

the specification of which is attached hereto unless the following box is checked:

☒ was filed on 20/Sep/00 as United States Application Number 10/070435 and was amended on 19/Mar/02 (if applicable) or,

PCT International Application Number
PCT/JP00/06399 and was amended on
(if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority under Title 35, United States Code §119(a-d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT international application which designated at least one country other than the United States, listed below. I have also identified below, by checking the "No" box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed:

Priority claimed
優先権の主張

☒ ☐
Yes No
あり なし

☐ ☐
Yes No
あり なし

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto.

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私は、合衆国法典第 35 部第 119 条 (e) 項に基づく、下記の合衆国仮特許出願の利益を主張する。

(Application No.)
(出願番号)

(Application No.)
(出願番号)

(Application No.)
(出願番号)

☐ その他の合衆国仮特許出願番号は別紙の追補優先権欄にて記載する。

私は、合衆国法典第 35 部第 120 条に基づく下記の合衆国特許出願、又は第 365 条 (c) 項に基づく合衆国を指名した PCT 国際出願の利益を主張し、本願の請求の範囲各項に記載の主題が合衆国法典第 35 部第 112 条第 1 項規定の態様で、先の合衆国特許出願又は PCT 国際出願に開示されていない限度において、先の出願の出願日と本願の国内出願日又は PCT 国際出願日の間に有効となった連邦規則法典第 37 部第 1 章第 56 条に記載の特許要件に所要の情報を開示すべき義務を有することを認める。

(Application No.)
(出願番号)

(Day/Month/Year Filed)
(出願の年月日)

(Application No.)
(出願番号)

(Day/Month/Year Filed)
(出願の年月日)

☐ その他の合衆国又は国際特許出願番号は別紙の追補優先権欄にて記載する。

私は、ここに自己の知識に基づいて行った陳述が全て真実であり、自己の有する情報および信ずるところに従って行った陳述が真実であると信じ、さらに故意に虚偽の陳述等を行った場合、合衆国法典第 18 部第 1001 条により、罰金もしくは禁に処せられるか、またはこれらの刑が併科され、またかかる故意による虚偽による陳述が本願ないし本願に対して付与される特許の有効性を損なうことがあることを認識して、以上の陳述を行ったことを宣言する。

私、下記署名者は、ここに記載の米国弁護士または代理人に本出願に関し特許商標庁にて取られるいかなる行為に関して、同米国弁護士又は代理人が私に直接連絡なしに私の外国弁護士或いは法人代表者からの指示を受け取り、それに従うようここに委任する。この指示を出す者が変更の場合には、ここに記載の米国弁護士又は代理人にその旨通知される。

I hereby claim the benefit under Title 35, United States Code §119 (e) of any United States provisional application(s) listed below.

(Day/Month/Year Filed)
(出願の年月日)

(Day/Month/Year Filed)
(出願の年月日)

(Day/Month/Year Filed)
(出願の年月日)

☐ Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

(現況) (Status)
(特許済み、係属中 放棄済み) (patented, pending, abandoned)

(現況) (Status)
(特許済み、係属中 放棄済み) (patented, pending, abandoned)

☐ Additional U.S. or international application numbers are listed on a supplemental priority sheet attached hereto.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

The undersigned hereby authorizes the U.S. attorney or agent named herein to accept and follow instructions from either his foreign patent agent or corporate representative, if any, as to any action to be taken in the Patent and Trademark Office regarding this application without direct communication between the U.S. attorney or agent and the undersigned. In the event of a change in the persons from whom instructions may be taken, the U.S. attorney or agent named herein will be so notified by the undersigned.

Japanese Language Utility or Design Patent Application Declaration

委任状： 私は、下記発明者として、下記に明記された顧客番号を伴う以下の弁護士又は、代理人をここに選任し、本順の手続きを遂行すること並びにこれに関する一切の行為を特許商標庁に対して行うことを委任する。そして全ての通信はこの顧客番号宛に発送される。

顧客番号 7055

現在委任された弁護士は下記の通りである。

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Japanese Language Utility or Design Patent Application Declaration

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国籍	Citizenship	
郵便の宛先	Post Office Address	

(それ以降の共同発明者に対しても同様な情報および署名を提供すること。)

(Supply similar information and signature for subsequent joint inventors.)